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**CERTIFICADA**

Re: International Patent Application N° PCT/EP03/13828

**Reply to the written opinion under Rule 66 PCT**

Dear Sirs,

First of all we must express our disappointment for what we interpret as a clear omission by the EPO of its duties as IPEA. You should bear in mind that you charge a huge amount of money for carrying out the IPE and that you must forward a reasoned WO under Rule 66.2(a)(ii). Your vague statements about the lack of novelty and inventive step of the set of claims under examination, without any argument, without citing which essential features of the claims affected by the prior art and, what is more important to allow applicant to duly reply, without detailing the arguments on which your statements of lack of novelty and inventive step lay on, have been somehow astonishing as they leaved us without any feed-back from your examination staff which we may use as guide-line, or clue to draft a response to the WO or, furthermore, to have an idea on how to amend the claims. Moreover, the WO is not even signed, neither any examiner is identified what, again, has left the applicant without the possibility of calling by phone to the examiner to exchange technical and legal criteria, to collect suggestions or to agree a draft response, pursuant, by way of example, Rule 66.6 PCT. That is the first time this has happened to us and we formally and respectfully, but firmly too, complain about that unjustified, in our view, behavior.

Coming back to the WO and in spite of the previous defaults in you WO communication, we shall do our best to reply to it by forwarding to you a set of amended claims which we believe, even though the lack of guidance given in the WO as already mentioned, they would overcome any objection raised about lack of novelty or inventive step.

#### Support for the amendments

Claim 1: The amended claim 1 is based in claim 1 as formerly filed. The value of the group R has been limited to the group hydroxi (OH), that was one of the options or preferred embodiments covered by former claim 2. That former claim 2, whose content has been introduced as essential feature of the amended claim 1, has, therefore, been removed.

The technical effect achieved by the ingestion of the food products claimed, have been amended by replacing the more general term "cardiovascular diseases" by hypertension. Support for that amendment may be found in the specification as formerly filed (pg.1, lines 5-10; pg. 6, lines 20-24; pg. 7, lines 1-4; pg. 12, lines 10-17 and Fig. 6). A new category of food has been added: functional food additive. That inclusion is supported in the specification as formerly filed (pg. 8, lines 21-25). The replacement of the term "and obesity" by "and/or obesity" is supported by Fig. 8 and pg. 14, lines 18-23 of the specification as formerly filed.

Claim 2: Amended claim 2 is based in former claim 3.

Claim 3: Amended claim 3 is based on former claim 4 which now, in view of the amended value claimed for the group R, has been limited to one of the preferred embodiments (2-hydroxyoleic acid).

Claim 4: Amended claim 4 is based on former claim 5, wherein the use as food has been limited to a specific compound (2-OH oleic acid) for the prevention and control of a specific disease: hypertension. Limitation of the general term "blood pressure and associated diseases" to "hypertension" is supported by the specification as formerly filed (pg. 12, lines 10-17).

Claim 5: Amended claim 5 is based on former claim 6, wherein the use as food has been limited to a specific compound (2-OH oleic acid) for the prevention and control of a specific disease: obesity. Limitation of the term "control of body weight" to obesity is supported by the specification as formerly filed (former claim 1). In any case, both terms are equivalent. "Prevention and control of obesity" should be interpreted as control of body weight (pg. 14, lines 18-23; Fig. 8) or as by food additive or so, getting a reduction of weight or, equally, causing weight loss (pg. 6, lines 21-24).

In our view, no new technical matter going beyond the content of the specification as formerly filed, has been introduced in the amended set of claims.

### Novelty

We have numbered the relevant prior art documents (cited under the "X" category), a task that usually is done by the IPEA, as follows:

D1: WO03/030891  
D2: WO92/21335  
D3: Meijer et al  
D4: US2003/157237

D1 is a previous IA in the name of the same applicant that present IA and discloses the use of the same family of compounds under the same Markush formula for preparing medicaments and pharmaceutical compositions.

D2 discloses phospholipids containing omega-3-fatty acids and its use for manufacturing nutrition emulsions giving low blood triglyceride and cholesterol levels. Specifically this prior art document discloses the use of 2 fatty acids: docosahexaenoic acid, 22:6w3 (DHA) and eicosapentaenoic acid, 20:5w3 (EPA).

D3 discloses the effect of dietary fat composition, fed to hamsters, based on triglycerides, comprising five fatty acids: elaidic (C18:1 9t), vaccenic (C18:1 11t), oleic (C18:1 9c), palmitic (C16:0) and a mixture of medium-chain fatty acids (MCFA: C8:0 and C10:0), on the development of blood cholesterol levels.

D4 discloses triglycerides used to reduce lipids blood levels. The triglycerides disclosed comprise at first and third carbons, saturated medium chain fatty acids having 8-10 carbons, and in the 2<sup>nd</sup> carbon, a monounsaturated long chain fatty acid having 16-18 carbons is chosen.

Claim 1 as now amended does not relate to any of the compounds disclosed either on D2, D3 or D4. None of those documents disclosed monounsaturated fatty acid hydroxy-derivatives, as the ones now claimed under the Markush formula of claim 1, wherein the value of the group R has been limited to a group -OH.

Concerning D1, the use of hydroxy-derivatives as the ones now claimed, is disclosed for preparing medicaments or pharmaceutical compositions, but not for manufacturing food additives and/or ingredients, dietary products food forms or food-stuff, in general, as amended claim 1 scopes, now covers. We would like to point out that the definition of dietary food product is specifically given in pg. 6, lines 24-27 of the specification as formerly filed as counter-position of what is understood by dosage for medical treatment. The present IA differs from D1, mainly in 2 figures (6 and 8) which were not present in D1 because there are figures dealing with dietary food ingestion instead of medical treatment dosages administered by injection. As it can be acknowledged, D1 discloses assays for reducing hypertension by medical treatment administration of 2-hydroxyoleic acid in

amounts of 1 mg and 10 mg, per kg of rat body weight, in acute or chronic treatment, respectively (See D1, pg. 18, lines 1-9) distributed in 3 injections per day ( $3 \times 10 \text{ mg} = 30 \text{ mg/kg}$  daily during 7 days in the chronic treatment; See D1, pg. 22, lines 11-22 and Fig. 9). However, present IA discloses diets of the same compound but used as food functional additive, by ingestion of 600 mg/kg every 12 h (See pg. 12, lines 10-17 and Fig. 6).

Hence, we may reasonably conclude that independent claim 1, as now amended, is novel over any of the D1-D4 cited prior art documents.

### Inventive step

D1 is considered the closest prior art because it deals with the use of a related family of compounds, for preparing medicaments. Those medicaments are said in D1 to be useful for achieving analogous technical effects to the ones achieved by the use claimed in the present application, as food additives, ingredients, etc...mainly: prevention and control of hypertension and obesity.

The technical problem solved by the present invention is to provide an advantageous technical effect to food compositions, to avoid or reduce the risks of developing hypertension and obesity. That technical problem is solved by the invention by including in the food the fatty acid OH-derivatives covered by the formula I of main claim 1, as amended.

D1 does not disclose the use of such a FA OH-derivatives for manufacturing foods, but only to use them for preparing pharmaceutical products with the therapeutic purposes inherently linked to any medicament. Moreover, all the assays disclosed for supporting the therapeutic effects achieved are expressed in terms of dosages and medical treatment. Those therapeutical doses being much lower than the concentration of FAs hydroxyderivatives now used as food functional additives. Moreover, the route of administration as medicaments (injection) has nothing to do with the inclusion in the diet of the claimed FAs OH-derivatives. Nothing is said or suggested, about using 2-OH-FAs derivatives, for achieving anti-hypertension or anti-obesity effects, used as ingredients of a diet. Thus, the hypotensive therapeutic effect achieved in rats with a treatment with 2-OH-oleic acid is expressed in dosage of mg of FA derivative per kg of rat body weight (10 mg/Kg in the chronic treatment, see D1 pg. 18, lines 1-9 and Fig. 9). Moreover, in the explanatory notes to Fig. 9 given in D1 (pg. 22, lines 11-16) is clearly mentioned that the treatment for reducing blood pressure in experimental rats is carried out by means of 3 injections per week in the chronic treatment which is the treatment that might resemble the most to a diet. The same happens for the therapeutic effects concerning obesity. Also the anti-obesity effect is expressed in terms of dosages and medical treatment for the assays performed in rats. In this effect, the rats had free access to food and water, which obviously imply that no diet enriched in 2-OH-oleic acid was provided to the experimental animals (See D1, pg. 19, lines 15-22 and Fig. 11). In the explanatory notes of D1, Fig. 11, given in pg. 22 line 31 to pg. 23, line 2, the dosage of 2-OH-oleic administered in the anti-obesity treatment (30 mg/kg) is also injected

(3 times daily) versus the 600 mg/kg every 12 h, given to experimental rats, as food supplement, in the diet (See pg. 14, lines 18-23; Fig. 8). Again no disclosure or suggestion is made in D1 in the sense that the technical effects observed when a medical treatment based in administering to the experimental animals, by daily injections, 2-OH-oleic acid, may be achieved by using such a compound as ingredient or additive of food. The man skilled in the art, departing from D1 could not find obvious that a medical compound which works in a medical treatment and which is administered by injection, will work efficiently if administered as ingredient in food. The digestive pathway barriers and enzymes would not make feasible that approach. As matter of fact, many therapeutic active compounds, like antibiotics, as a way of example, that work efficiently when administered by injection, would never work whether they were used as food ingredients or additives. Most medicaments have ever form part of food-stuffs.

When the man skilled in the art would depart from the teaching disclosed in D1, he would be confronted to the previously mentioned technical problem that, something that works as medicament administered by injection, can likely not work, from the point of view of achieving analogous technical effects (Anti-hypertensive and/or anti-obesity), if the same active principle is used for preparing foods. D2 could not help much to reach the solution found in the invention, as far as D2 concerns phospholipids with a high amount of polyunsaturated FAs (DHA and EPA) which are unrelated compounds with regard to the monounsaturated FA hydroxi-derivatives, as now claimed. Then, in our view, a combination D1+D2, could never lead to the man skilled in the art to the solution claimed in independent amended claim 1.

Something similar could happen to the man skilled in the art if he would try to combine D1+D3. That other prior art document (D3) discloses diets based of triglycerides and the FAs mixed with those triglycerides are not FAs OH-derivatives, as the ones claimed. We found hardly to believe that a combination of D1+D3 under actual circumstances could render obvious the characterizing portion of amended claim 1.

The same occurs when a combination of D1+D4 is used for judging inventive step of the claimed invention. D4 discloses also triglycerides in which at least their 1<sup>st</sup> and 3<sup>rd</sup> carbons are saturated medium chain FAs having 8-10 carbons, which do not have nothing to do with the FAs OH-derivatives now claimed. In our view, the man skilled in the art could never be persuaded, by departing of D1 teaching, by D4 content, to assay FAs OH-derivatives, as the one now claimed, in food compositions to prevent or control hypertension and/or obesity.

Therefore, we believe that independent use claim 1, as now amended, meets the novelty and inventive step PCT requirements, over the cited prior art D1-D4.

Notwithstanding previous statement, this representative, would like to request, an informal communication with the examiner pursuant to Rule 66.6 PCT, whether, in spite of the present reply and accompanying amendments in the set of claims, the examiner would still have any doubt or question to be asked. We also respectfully request, under Rule 66.4 to

have an additional opportunity to submit further amendments whether the examiner would keep on thinking that the set of claims enclosed hereto, it still fails in any patentability requirement or if any formal error, mistake or omission, may be worked out, to leave the IA in good order for allowability when entered into the different national phases.

Yours faithfully,

E L Z A B U R U

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Alberto de Elzaburu, P.P.

Enclosures:

Set of amended claims 1-6 (Replacement page 18)